

U.S.S.N. 09/586,625
BARBAS III *et al.*
AMENDMENT

D60
regulating domain. The nucleotide binding domain is a zinc-finger peptide that binds to a targeted contiguous nucleotide sequence of from 3 to about 18 nucleotides are provided. The fusion proteins are used for gene therapy. Also provided are polynucleotides encoding the fusion proteins, expression vectors, and transfected cells.

IN THE CLAIMS:

Please replace claims 1, 8, 13, 20, 22, 25, 32, 39, 43, 45, 69 and 73 with amended claims 1, 8, 13, 20, 22, 25, 32, 39, 43, 45, 69 and 73 as follows:

1. (Amended twice) A fusion protein, comprising a nucleotide binding domain operatively linked to a ligand binding domain from an intracellular receptor, wherein:

D61
the nucleotide binding domain is a polydactyl zinc-finger peptide or modular portion thereof that interacts with a contiguous nucleotide sequence of at least about 3 nucleotides;

the ligand binding domain has been modified to change its ligand specificity compared to the native hormone receptor; and

the fusion protein is a ligand activated transcriptional regulator.

8. (Amended three times) A fusion protein, comprising a nucleotide binding domain operatively linked to a ligand binding domain from an intracellular receptor, wherein:

D62
the nucleotide binding domain is a polydactyl zinc-finger peptide or modular portion thereof that interacts with a contiguous nucleotide sequence of at least about 3 nucleotides;

the zinc-finger peptide is comprised of modular units from a C2H2 zinc-finger peptide that interacts with a sequence of nucleotides and targets the fusion protein to an exogenous or endogenous gene that comprises the sequence of nucleotides; and

the fusion protein is a ligand activated transcriptional regulator.

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D63
13. (Amended twice) The fusion protein of claim 3, wherein the hormone receptor is a progesterone receptor variant or an estrogen receptor variant, wherein a receptor variant comprises a ligand binding domain that has altered ligand specificity for endogenous and exogenous ligands relative to its native receptor.

20. (Amended twice) A fusion protein, comprising a nucleotide binding domain operatively linked to a transcription regulating domain and a ligand binding domain from an intracellular receptor, wherein:

D64
the nucleotide binding domain is a polydactyl zinc-finger peptide or modular portion thereof that interacts with a contiguous nucleotide sequence of at least about 3 nucleotides;

the transcription regulating domain comprises a transcription repression domain; and

the fusion protein is a ligand activated transcriptional regulator.

22. (Amended twice) A fusion protein, comprising a nucleotide binding domain operatively linked to a transcription regulating domain and a ligand binding domain from an intracellular receptor, wherein

D65
the nucleotide binding domain is a polydactyl zinc-finger peptide or modular portion thereof that interacts with a contiguous nucleotide sequence of at least about 3 nucleotides;

the fusion protein is a ligand activated transcriptional regulator; and the fusion protein is encoded by the sequence of nucleotides set forth in any of SEQ ID Nos. 1-18.

25. (Amended three times) A nucleic acid molecule, comprising a sequence of nucleotides encoding a fusion protein, wherein:

D66
the fusion protein comprises a nucleotide binding domain operatively linked to a ligand binding domain from an intracellular receptor, wherein the nucleotide binding domain is a polydactyl zinc-finger peptide or modular portion thereof that interacts with a contiguous nucleotide sequence of at least about 3 nucleotides;

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D66
the fusion protein is a ligand activated transcriptional regulator; and
the fusion protein is encoded by a sequence of nucleotides set forth in
SEQ ID No. 1.

32. (Amended twice) A viral vector comprising a sequence of
nucleotides encoding a fusion protein, wherein:

D67
the fusion protein comprises a nucleotide binding domain operatively
linked to a ligand binding domain from an intracellular receptor, wherein the
nucleotide binding domain is a polydactyl zinc-finger peptide or modular portion
thereof that interacts with a contiguous nucleotide sequence of at least about 3
nucleotides; and

the fusion protein is a ligand activated transcriptional regulator.

39. (Amended twice) A combination, comprising:

D68
a fusion protein comprising a nucleotide binding domain operatively
linked to a ligand binding domain from an intracellular receptor, wherein
the nucleotide binding domain is a polydactyl zinc-finger peptide or modular
portion thereof that interacts with a contiguous nucleotide sequence of at least
about 3 nucleotides and the fusion protein is a ligand activated transcriptional
regulator; or

a nucleic acid molecule comprising a sequence of nucleotides that
encodes the fusion protein; and

a regulatable expression cassette that comprises at least one
response element recognized by the nucleic acid binding domain of the fusion
protein.

43. (Amended twice) A composition for regulating gene expression,
comprising an effective amount of:

D69
a fusion protein comprising a nucleotide binding domain operatively linked
to a ligand binding domain from an intracellular receptor, wherein the nucleotide
binding domain is a polydactyl zinc-finger peptide or modular portion thereof
that interacts with a contiguous nucleotide sequence of at least about 3

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nucleotides and the fusion protein is a ligand activated transcriptional regulator;
or

69
D a nucleic acid molecule comprising a sequence of nucleotides that
encodes the fusion protein; and

a pharmaceutically acceptable excipient.

45. (Amended twice) A composition for regulating gene expression
comprising an effective amount of:

40
D a fusion protein comprising a nucleotide binding domain operatively linked
to a transcription regulating domain and a ligand binding domain from an
intracellular receptor, wherein the nucleotide binding domain is a polydactyl zinc-
finger peptide or modular portion thereof that interacts with a contiguous
nucleotide sequence of at least about 3 nucleotides and the fusion protein is a
ligand activated transcriptional regulator; and

a pharmaceutically acceptable excipient.

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D 69. (Amended) The fusion protein of claim 1, wherein the polydactyl
zinc-finger peptide or modular portion thereof interacts with a contiguous
nucleotide sequence of at least about 3 nucleotides to about 18 nucleotides.

72
D 73. (Amended) The fusion protein of claim 9, wherein the zinc finger
peptide comprised of at least one zinc finger or a variant thereof binds to a
targeted nucleic acid molecule with a dissociation constant of less than about
1.0 nanomolar.

REMARKS

A check for the fee for a three month extension of time accompanies this
response. Any other fees that may be due in connection with filing this paper or
with this application, including any excess fees for the addition of independent
claims herein, may be charged to Deposit Account No. 50-1213. If a Petition
for Extension of time is needed, this paper is to be considered such Petition.

Claims 1-3, 5-35, 37-46 and 69-73 are pending. Claims 1, 8, 13, 20,
22, 25, 32, 39, 43, 45, 69 and 73 are amended to more particularly point out
the claimed subject matter. Claim 25 is amended to address the Examiner's